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HUMAN METAPNEUMOVIRUS: AN EMERGING RESPIRATORY PATHOGEN

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□ **Abstract—Human metapneumovirus (hMPV) is an important emerging respiratory pathogen, previously unreported in the Emergency Medicine literature. It is primarily associated with the clinical syndromes of bronchiolitis and pneumonia. hMPV may predispose to bacterial pneumonia; coinfection with respiratory syncytial virus may lead to increased severity of clinical disease, and complications include asthma and chronic obstructive pulmonary disease exacerbations. Given its high prevalence and potential clinical implications as these patients present to the Emergency Department with initial infection or subsequent complications, a better understanding of hMPV will aid in their care. We report the case of a 13-month old who developed lobar pneumonia 3 weeks after being diagnosed with hMPV. The epidemiology, clinical presentation, complications, and treatment of hMPV are then discussed. © 2010 Elsevier Inc.**

□ **Keywords—human metapneumovirus; bronchiolitis; pneumonia; upper respiratory infection; lung**

INTRODUCTION

Human metapneumovirus is a newly discovered ubiquitous pathogen causing lower respiratory disease in both children and adults (1). Despite being well reported in the infectious disease and pediatric literature, there are no reports of this virus in the Emergency Medicine literature to date (1–8). More than 11 million patients with respiratory chief complaints account for 10.7% of all patients presenting to US Emergency Departments (9). Therefore, knowledge of the epidemiology, clinical presentation, and complications of human metapneumovirus is essential to the Emergency Physician.

The opinions and assertions contained herein are the private views of the authors and should not be construed as official or as reflecting the views of the Department of Army or the Department of Defense.

CASE REPORT

A 13-month-old girl was brought to our Emergency Department (ED) by her parents with a chief complaint of fever, wheezing, and increased work of breathing. Three weeks earlier she had been diagnosed with human metapneumovirus (hMPV) via real time-polymerase chain reaction (RT-PCR) as a part of a research protocol after presenting to her primary pediatrician afebrile with rhinorrhea and non-productive cough. No chest radiograph was obtained at that time. The cough persisted and the day before presentation to the ED she developed a maximum temperature of 38.4°C (101.2°F) orally, increasing cough, and audible wheezing. She had no other significant past medical or birth history, no allergies, and was taking no medications. Her parents denied apnea, cyanosis, increased drooling, foreign body ingestion, decreased level of consciousness, vomiting, or diarrhea.

Initial vital signs were a temperature of 36.9°C (98.5°F) orally, heart rate of 174 beats/min, respiration rate 44

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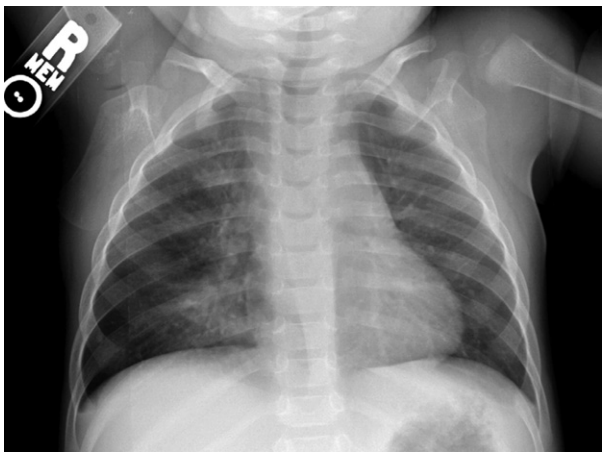

Figure 1. Posteroanterior chest radiograph demonstrating a right middle lobe infiltrate.

breaths/min, and an oxygen saturation of 95% on room air. Initial examination revealed an alert, well-hydrated female with bilateral rales and wheezing but no retractions, flaring, grunting, or stridor. There was no pharyngeal erythema, asymmetry, or exudate. Other than initial tachycardia, examination of the cardiovascular, abdominal, and skin systems were within normal limits.

The patient was initially treated with nebulized albuterol and prednisilone. Nasopharyngeal viral direct fluorescent antibody testing was negative for adenovirus, influenza A and B, parainfluenza virus 1, 2, and 3, and respiratory syncytial virus (RSV). Chest radiograph demonstrated a right middle lobe infiltrate and small right pleural effusion consistent with lobar pneumonia (Figure 1). Upon reexamination 90 min after albuterol therapy, she was breathing comfortably with no wheezing, improved oxygenation, and respiratory rate. The lobar infiltrate was assumed to be bacterial superinfection and she was treated with pediazole (erythromycin + sulfasoxazole) orally. Pediatric follow-up was arranged for the following day and she was discharged from the ED with her parents. Her post-ED recovery was uncomplicated.

DISCUSSION

Human metapneumovirus was first discovered in 2001 as another causative agent of acute respiratory tract infections in children (10). Since that time, hMPV has been described as a major respiratory pathogen in children, the elderly, and the immunocompromised (1). As these patients present to the ED with initial infection or subsequent complications, a better understanding of hMPV will aid in their care.

hMPV is a paramyxovirus classified within the subfamily *pneuomovirinae* (11). This subfamily includes RSV, which shares many epidemiological and clinical characteristics with hMPV. Large amounts of heterogeneity within its genome may account for incomplete immunity and recurrent infections that are often seen with this virus (2–4). Seroprevalence studies have shown that this virus has been circulating among the human population for 50 years and virtually all children older than 5 years show serologic evidence of past infection (1). The age distribution is bimodal, with children < 5 years old and adults aged > 65 years accounting for 35.1% and 45.9% of infections, respectively (2,3). hMPV infection is highly seasonal, with 86.7% of all hMPV-positive cultures being isolated between December and May (5).

The respiratory system is predominately affected by hMPV infection. In children, the syndrome seen with this virus is very similar to RSV infection and includes high fever, severe cough, increased work of breathing, and wheezing (6). After RSV, hMPV is one of the leading causes of bronchiolitis. Positive viral cultures have been seen in 5–10% of hospitalized children with acute respiratory tracts infections (ARTIs), as well as 12–15% of outpatients with ARTIs (3,6,7,12). Despite a higher incidence of wheezing with hMPV than with RSV, the severity of hMPV is usually less, with a lower incidence of hypoxemia, pneumonia, and Intensive Care Unit (ICU) admissions (2,6,8,13,14). Severe cases are seen in children between 3 and 6 months of age, as opposed to 0–2 months with RSV infections (6,13). Of note, the virus has also frequently been isolated from the nasopharnyx of children suffering from otitis media (6,8).

Given that hMPV is a ubiquitous virus with widespread seroconversion by age 5 years, adult illness is presumed to be the result of re-infection. The presentation of hMPV in adults is quite similar to the symptoms seen in young children, with a few noteworthy exceptions. Unlike the pediatric presentation, fever is rarely present. Symptoms primarily involve the upper respiratory tract, with congestion, cough, and rhinorrhea being the most prevalent (1). The highest incidence of infection is found in young adults, yet the elderly patients with multiple comorbidities have the most clinically significant infections. Dypsnea, wheezing, and hypoxia are usually confined to the elderly and immunocompromised, who present with bronchitis or pneumonitis. In Rochester, New York, 11% of hospitalized adult patients with acute respiratory infections had an associated hMPV infection (1). Exacerbation of chronic obstructive pulmonary disease (COPD) due to hMPV also contributes to the increased severity of illness in the elderly. Martinello et al. recently demonstrated a 12% incidence of hMPV infection in patients admitted with a COPD exacerbation (15).

Similar to other common viruses, hMPV infection may predispose the host to bacterial pneumonia. An increase in host susceptibility to pneumococcal infection due to infection with influenza virus, parainfluenza virus type 3, and RSV has been shown in animal and in vitro studies (16). In African children without human immunodeficiency virus, Madhi et al. were able to decrease the incidence of hospitalization for pneumonia associated with influenza A virus by 39%, pneumonia associated with parainfluenza virus types 1–3 by 44%, and pneumonia associated with RSV by 32% by immunizing children with 9-valent pneumococcal polysaccharide-protein conjugate vaccine (PCV) (17). These findings suggest that viral infections predispose to pneumococcal coinfection. Bacterial pneumonia coinfection with hMPV was first reported by Boivin et al. in two Canadian children hospitalized for acute respiratory illness. Isolated organisms were *Staphylococcus aureus* and *Streptococcus pneumoniae* (2). Similar to their previous study with other viruses, Madhi et al. recently reported a 58% overall reduction in the incidence of pneumonia associated with hMPV by immunizing with PCV (18). The authors suggest that this is "a conservative estimate of the prevalence of pneumococcal coinfection in children with hMPV" (18).

Other associated diseases are also of significance. In addition to bacterial coinfection, simultaneous infection with RSV and hMPV may lead to increased severity of disease compared with either virus alone. In one series of patients admitted to the ICU with positive hMPV cultures, 75% were also positive for RSV (19). hMPV may also be a significant inciting agent of asthma exacerbations. The incidence of acute asthma exacerbation after hMPV infection has been measured at 8–14% (2,3,14,20). There also have been reports of detection of hMPV in patients with severe acute respiratory syndrome (SARS), which adds this virus to the list of potentially lethal pathogens. However, a definitive correlation has yet to be established (3,4,21,22). Finally, a fatal case of encephalitis in an infant has also been reported (23). Although these associations are in the preliminary stages, as testing for this virus becomes more readily accessible, the impact of hMPV on the ED is likely to be established.

Testing for the virus is via RT-PCR, as immunofluorescence and viral culture techniques are not clinically available. RT-PCR is currently being used, mostly for epidemiology research and occasionally in the pediatric ICU setting. RT-PCR amplifies hMPV RNA in nasopharyngeal sections, allowing detection of the active virus from a combined nose and throat swab or nasopharyngeal aspirate. This test identifies only current infection, given that the previously infected patient does not have live viral RNA in their nasopharynx. A batched PCR assay that identifies RSV, influenzavirus, parainfluenzavirus 1–4, rhinoviruses, adenoviruses, human coronaviruses OC43, NL63, and 229E, hMPV, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae* is used for this purpose (24). Although its use is increasing, this test is not yet widely available in EDs.

Symptomatic treatment is the standard approach for patients with hMPV. The effect of corticosteriods, antivirals, and supportive measures is yet to be determined. Ribavirin has shown similar antiviral activity against both RSV and hMPV in vitro. Intravenous immunoglobulins have also showed inhibitory activity in vitro, however, no drug or treatment regime against hMPV has been tested in vivo (25). Live, attenuated viruses have been used effectively as vaccines in animal models, but no vaccine has been used in humans (26).

As a widespread virus causing bronchiolitis and pneumonitis, inciting asthma and COPD exacerbations, likely predisposing to bacterial pneumonia, and possibly related to severe illness such as SARS and encephalitis, hMPV is an emerging respiratory pathogen of which no Emergency Physician should be completely unaware. Currently, RT-PCR testing for hMPV in the ED is not available or necessary, as it will not change the management of associated clinical syndromes. However, as ongoing research further develops our understanding of this virus and its impact on our patients' clinical course, changes in admission criteria, treatment, follow-up planning, and return precautions due to infection with the virus may emerge.

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